Complete Summary

GUIDELINE TITLE

ACR Appropriateness Criteria™ for pretreatment staging of clinically localized prostate cancer.

BIBLIOGRAPHIC SOURCE(S)

American College of Radiology (ACR), Expert Panel on Urologic Imaging. Pretreatment staging of clinically localized prostate cancer. Reston (VA): American College of Radiology (ACR); 2003. 5 p. (ACR appropriateness criteria). [28 references]

GUIDELINE STATUS

This is the current release of the guideline.

All Appropriateness Criteria™ are reviewed annually and updated as appropriate.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

Prostate cancer

GUIDELINE CATEGORY

Diagnosis
Evaluation

CLINICAL SPECIALTY

Oncology
Radiology
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide appropriate recommendations for pretreatment staging of patients with clinically localized prostate cancer

TARGET POPULATION

Patients with clinically localized prostate cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation*

1. Magnetic resonance imaging (MRI) with or without proton spectroscopy (MRSI)
2. Computed tomography of pelvis/abdomen
3. Transrectal sonography (TRUS)
4. Radionuclide bone scan
5. ProstaScint radio-immunodetection

*Note that staging of prostate cancer uses a multimodal approach, which also includes measurement of prostate-specific antigen (PSA), and consideration of the patient's age and Gleason score.

MAJOR OUTCOMES CONSIDERED

Staging accuracy of radiography, computed tomography, proton spectroscopy, radionuclide bone scan, radio-immunodetection and magnetic resonance imaging procedures for prostate cancer

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of recent peer-reviewed medical journals, primarily using the National Library of Medicine's MEDLINE database. The developer identified and collected the major applicable articles.

NUMBER OF SOURCE DOCUMENTS

The total number of source documents identified as the result of the literature search is not known.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed to reach agreement in the formulation of the Appropriateness Criteria. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by the participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1-9, indicating the most to the least appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty (80) percent agreement is considered a consensus. If consensus cannot be reached by this method, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Task Force on Appropriateness Criteria and the Chair of the ACR Board of Chancellors.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria™

Clinical Condition: Pretreatment Staging of Clinically Localized Prostate Cancer

Variant 1: PSA 10 ng/ml or less; and/or Gleason Score 2–6

Radiologic Exam Procedure	Appropriateness Rating	Comments
Magnetic resonance imaging (MRI)	4	
Computed tomography (CT) of pelvis/abdomen	4	
Transrectal sonography (TRUS)	4	
Radionuclide bone scan	2	
Appropriateness Criteria Scale		
1 2 3 4 5 6 7 8 9		
1=Least appropriate 9=Most appropriate		

Variant 2: PSA > 10 ng/ml; and < 20, and/or Gleason Score 7

Radiologic Exam Procedure	Appropriateness Rating	Comments
Radionuclide bone scan	8	
Computed tomography (CT) of pelvis/abdomen	8	
MRI +/- MRSI (proton spectroscopy)	6	Not yet widely available. Spectroscopy technique is still

Radiologic Exam Procedure	Appropriateness Rating	Comments
		evolving. Requires experienced observer.
ProstaScint radio-immunodetection	4	Not yet widely available. Requires skill in interpreting SPECT. Relatively expensive.
Transrectal sonography (TRUS)	4	
Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1=Least appropriate 9=Most appropriate		

Variant 3: PSA >20 ng/ml; and/or Gleason Score > 8

Radiologic Exam Procedure	Appropriateness Rating	Comments
Radionuclide bone scan	8	
MRI +/- MRSI	8	
Computed tomography (CT) of pelvis/abdomen	8	
ProstaScint radio-immunodetection	4	Not yet widely available. Requires skill in interpreting SPECT. Relatively expensive.
Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1=Least appropriate 9=Most appropriate		

Prostate cancer is an exceedingly common malignancy. It is now the most common noncutaneous malignancy of men in the United States and is the second leading cause of death by cancer in American men. It is commonly recommended that men over the age of 50 have an annual digital rectal examination (DRE) and a prostate-specific antigen (PSA) blood level analysis. If either of these suggests neoplasm, needle biopsy of the prostate gland is usually performed under sonographic guidance. Another method of diagnosing prostate cancer is finding the disease in the chips removed during a transurethral resection of the prostate for presumed benign disease. Clinically localized disease (Stage T1 or T2) is generally amenable to local cure. Treatment methods include radical prostatectomy and radiation therapy. Tumor transgressing the capsule into the periprostatic space, even if microscopic, is considered Stage C disease. Such patients are not candidates for curative therapy and are usually treated with hormonal manipulation.

Cancer Staging

PSA (a monoclonal antibody assay) is used as a biomarker, not only in identifying men with prostatic cancer but also in predicting pathologic stage, especially when combined with patient´s age and Gleason sum. In general the higher the PSA, the more advanced the disease; moreover, the likelihood of having organ-confined disease is inversely proportional to the level of the PSA. PSA measurements are evaluated alone or by comparison with a prior measurement (PSA velocity) or in the context of the patient's gland volume (PSA density). There are also age-specific PSA levels available. In the latter two, the density and age specificity help to separate the elevations in PSA due to benign prostatic hyperplasia (BPH). The other newer way of evaluating PSA is to measure the two components, the free and bound; the proportion of free PSA is lower in patients with cancer, than in BPH. Tumor grade also correlates reasonably well with pathologic stage. The Gleason grading system ranges from 2 (well differentiated, minimally aggressive) to 10 (anaplastic, highly malignant). However, the capability of PSA level and/or a high Gleason Score alone to accurately predict final pathologic stage on an individual basis has a prohibitively high false-positive rate. Therefore, many physicians rely on a multimodal approach including imaging examinations to predict pathologic stage before treatment. A method reported to predict prostate-specific antigen (PSA) failure free survival following either radical prostatectomy (RP) or conventional dose (i.e., 70 Gray) 3D conformal external beam radiation therapy (3DCRT) for patients with clinically localized prostate cancer is called "combined modality staging." The methodology identifies the set of independent pretreatment clinical predictors of PSA outcome in order to categorize patients who are likely (i.e., low-risk) or unlikely (i.e., high-risk) to achieve long term cancer control following RP, brachytherapy or conventional dose 3DCRT. Using these risk groups as the baseline provides the framework on which to ascertain whether a new test provides further stratification of PSA outcome beyond that already provided by the established predictors. Particular attention needs to be given to the patients classified in the intermediate risk group that comprise approximately one third of all patients with clinically localized prostate cancer and where improvement in the prediction of PSA outcome is most needed.

Studies evaluating men diagnosed with prostate cancer during the PSA era have shown that the PSA, Gleason score, and the 1992 American Joint Committee on Cancer (AJCC) clinical T-stage provide independent information regarding PSA outcome following local therapy. Based on a review of the literature, three risk groups can be defined as follows:

Low Risk:

- 2002 AJCC clinical stage $T_{1c, 2a}$ and PSA $\leq$ 10 ng/ml and biopsy Gleason score $\leq$ 6
- ~ 80 % 10-year PSA failure free survival

Intermediate Risk:

- 2002 AJCC clinical stage T_{2b} or PSA > 10 and $\leq$ 20 ng/ml or biopsy Gleason score 7
- ~ 50% 10-year PSA failure free survival

High Risk:

- 2002 AJCC stage T_{2c} disease or PSA > 20 ng/ml or biopsy Gleason score $\geq$ 8
- ~ 33% 10-year PSA failure free survival

The experience with transrectal ultrasound (TRUS) in staging prostate cancer is variable. Recent work using color Doppler sonography indicates that this may be helpful for tumor identification with improvement over standard gray scale US. The TRUS has been touted as an acceptable method of staging prostate cancer by differentiating patients who have confined disease from those with more advanced disease. Unfortunately, the results are not always reproducible. For example, one study found the predictive value for tumor confinement by TRUS to be 37% and another study found TRUS correctly staged only 46% of localized disease; however, yet another study reported an accuracy of 83% for sonographic detection of extra-capsular penetration. Summarizing the role of TRUS in staging prostate cancer, it appears generally more accurate than CT in detecting extracapsular penetration.

Abdominopelvic CT is occasionally used to preoperatively stage prostate cancer. Multiple studies have indicated a poor accuracy for CT in staging this disease. Overall accuracy in staging was reported as 65% by Hricak et al and as 67% by Platt et al. For locoregional staging, such as extracapsular penetration, the accuracy has been reported as low as 24%. Even with refined techniques in performing CT (3 mm slice thickness and 5 mm table increments with both intravenous and oral contrast), it has been concluded that CT is of little value in staging the local extent of prostatic carcinoma. However, one study reports 93.7% accuracy for CT in detecting positive lymph nodes, which increases to 96.5% if CT-guided fine-needle aspiration biopsy is added. This degree of accuracy was obtained by considering every node 6 mm or larger as pathologic; this is a departure from previous CT criteria for positive nodes. This, however, is an impractical stance and is not widely followed in the U.S. Summarizing the current use of CT in staging prostate cancer, it appears to have little value in determining the direct extension of the tumor, but if the newer criterion for positive nodes is adopted, it may prove to be accurate in detecting nodal disease.

Several investigators have shown the reliability of the endorectal coil magnetic resonance imaging (erMRI) to predict pathologic stage. It has been shown to be somewhat related to the imaging technique and the experience of the individual MR radiologist. There has been an improvement in the staging efficacy of MRI for prostate cancer by the use of endorectal coils. Original studies report a prospective overall staging accuracy, using endorectal coils, of 51% and a retrospective staging accuracy of 67%. These findings were replicated by yet another group who reported a 68% overall staging accuracy, though earlier work by the same group had indicated that endorectal coil imaging was 82% accurate in the differentiation of Stage B from Stage C cancer. The RDOG data sets and others were used to evaluate a method to improve inter-reader variability by Seltzer et al. Using two groups of radiologists, prostate MR experts and body MR radiologists, they showed a significant improvement in the baseline performance of the body MR radiologists, from an ROC Az (the area under the ROC curve, maximum value is 1.0) of 0.6 to 0.8. Interestingly in this study, the expert radiologist had a baseline ROC Az of 0.83. Thus, this is an accurate test in experienced hands and can be improved in others with learning enhancements.

Getty et al have expanded on this and shown the increased value of MRI in the previously defined intermediate risk group of men. Given this information, a different question was asked using the combined modality staging methodology. Specifically, in the group of men with intermediate risk prostate cancer that were not classifiable into a low or high-risk cohort, did the erMRI T-stage (right or wrong) provide clinically significant information regarding PSA outcome following RP? The results suggested that the erMRI T-stage may have clinical utility in this select subgroup of intermediate-risk patients for predicting PSA outcome following RP. Specifically, for those patients the 5-year PSA outcome stratified by the erMRI T-stage was 72% (T2) vs. 33% (T3). These results must be viewed with caution; however, because unlike the percent positive prostate biopsy information, they have not been validated. In addition they were achieved utilizing an expert prostate MR radiologist and the study has not been performed for patients managed using RT. Therefore, the results will need to be validated using an independent RP and RT database utilizing more than a single expert MR radiologist.

MR has also been shown to be at least equivalent, if not better than CT for the detection of abnormal lymph nodes in men with prostate cancer. Proton spectroscopy (MRSI) has been evaluated and found useful for the detection and diagnosis of prostate cancer, as well as an aid in staging. The role of spectroscopy, for improving staging prior to radical prostatectomy, is under prospective study by the American College of Radiology Imaging Network (ACRIN). It has been reported to be useful for cancer diagnosis and detection after treatment such as chemotherapy or cryotherapy. Capromab pendetide radiolabeled with indium-111 (ProstaScint; Cytogen Corp., Princeton, NJ) is a radioimmunoscintigraphic agent that may be useful staging patients with prostate cancer. This monoclonal antibody has been investigated in patients with clinically localized disease but who are considered at high risk for metastases because of elevated PSA levels or high Gleason Score. A review of two recent multicenter clinical trials found a sensitivity of 52 and 62% and a specificity of 72 and 96% as confirmed by pelvic lymphadenectomy results. When used in conjunction with other diagnostic methods, ProstaScint offers the possibility of defining the extent of disease in high-risk (PSA greater than 10 ng/ml), newly diagnosed prostate cancer patients.

Summary

Staging of prostate cancer should use a combined modality approach using PSA (a monoclonal antibody assay), Gleason, number of positive biopsies and patient´s age. The likelihood of direct extension or distant metastases is low in patients with low-grade tumors and low levels of PSA. Patients with tumors with high-elevated PSA levels, or Gleason scores have a high risk of capsular transgression, positive nodes, or bony metastases. Therefore, even in the face of a digital rectal exam (DRE) that suggests localized disease, such patients should have a more detailed preoperative staging evaluation. Magnetic resonance imaging (MRI) using endorectal coil techniques is the most useful imaging test available, providing both locoregional and nodal evaluation. Experienced radiologists can be very accurate when using this technique. Proton spectroscopy (MRSI) has the potential to improve the overall accuracies even further. Patients with intermediate risk factors or a discordant variable will benefit most from imaging with endorectal coil MRI. In high-risk patients with a PSA over 10ng/mlradionuclide bone scans are

useful for detecting bony metastases. ProstaScint may also play a role in detecting nodal metastases.

Anticipated Exceptions

None

CLINICAL ALGORITHM(S)

None provided

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

POTENTIAL BENEFITS

Appropriate use of imaging studies in the pretreatment staging of clinically localized prostate cancer

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

An American College of Radiology (ACR) Task Force on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other coexistent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the United States Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific

radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American College of Radiology (ACR), Expert Panel on Urologic Imaging. Pretreatment staging of clinically localized prostate cancer. Reston (VA): American College of Radiology (ACR); 2003. 5 p. (ACR appropriateness criteria). [28 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Radiology

GUIDELINE COMMITTEE

Expert Panel on Urologic Imaging

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Clare Tempany, MD; Peter L. Choyke, MD; William H. Bush, Jr, MD; Syed Z. H. Jafri, MD; Robert A. Older, MD; Arthur T. Rosenfield, MD; Arthur J. Segal, MD; Martin I. Resnick, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

All Appropriateness Criteria™ are reviewed annually and updated as appropriate.

GUIDELINE AVAILABILITY

Electronic copies: Available Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on November 15, 2004. The information was verified by the guideline developer on December 21, 2004.

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Date Modified: 2/14/2005

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